

W110720010.ST25.txt
SEQUENCE LISTING

<110> Williams, Kevin J.
<120> Thrombospondin Fragments and Uses Thereof In Clinical Assays for
Cancer and Generation of Antibodies and Other Binding Agents
<130> W1107-20010
<140> 10/525,610
<141> 2003-08-20
<160> 64
<170> PatentIn version 3.3
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Thr Glu Glu Asn Lys Glu
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<400> 2

Cys Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu Asn Lys Glu
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Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu Asn Lys Glu
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Glu Gly Glu Ala Arg Glu
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Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu
1 5 10

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Glu Asp Thr Asp Leu Asp
1 5

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Tyr Ala Gly Asn Gly Ile Ile Cys Gly Glu Asp Thr Asp Leu Asp
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Cys Asn Ser Pro Ser Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu
Page 2

1 5 15

Ala Arg

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Arg Lys Val Thr Glu Glu Asn Lys Glu Leu Ala Asn Glu Leu Arg Arg
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Pro

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aid conjugation

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Cys Arg Lys Val Thr Glu Glu Asn Lys Glu Leu Ala Asn Glu Leu Arg
1 5 10 15

Arg Pro

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Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg
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Cys Glu Gly Glu Ala Arg
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Arg Lys Val Thr Glu Glu Asn Lys Glu
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Asp Asp Asp Asp Asn Asp Lys Ile Pro Asp Asp Arg Asp Asn Cys
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Asp Asp Asp Asp Asn Asp Lys
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Asn Leu Pro Asn Ser Gly Gln Glu Asp Tyr Asp Lys Asp Gly
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Glu Asp Tyr Asp Lys Asp
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Cys Pro Tyr Asn His Asn Pro Asp Gln Ala Asp Thr Asp Asn Asn Gly
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Glu Gly Asp

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Cys Arg Leu Val Pro Asn Pro Asp Gln Lys Asp Ser Asp Gly Asp
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Asp Gln Lys Asp Ser Asp Gly Asp
 1 5

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Cys Pro Tyr Val Pro Asn Ala Asn Gln Ala Asp His Asp Lys Asp Gly
 1 5 10 15

Lys Gly Asp Ala
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Thr Glu Arg Asp Asp Asp
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Asp Phe Ser Gly Thr Phe Phe Ile Asn Thr Glu Arg Asp Asp Asp
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<400> 26

Glu Arg Lys Asp His Ser
1 5

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Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His Ser
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Cys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His Ser
1 5 10 15

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<400> 29

Asp Asp Lys Phe Gln Asp

1 5

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Ala Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp
1 5 10

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Cys Ala Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp
1 5 10 15

<210> 32
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<400> 32

Asp Cys Glu Lys Met Glu
1 5

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Glu Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn
1 5 10 15

<210> 34
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Cys Gly Thr Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe
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Asp

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<400> 35

Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp
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Gly Trp Lys Asp Phe Thr Ala Tyr Arg Trp Arg Leu Ser His Arg Pro
1 5 10 15

Lys Thr Gly

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Cys Gly Trp Lys Asp Phe Thr Ala Tyr Arg Trp Arg Leu Ser His Arg
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Pro Lys Thr Gly
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<400> 38

Met Gly Leu Ala Trp Gly Leu Gly Val Leu Phe Leu Met His Val Cys
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Gly Thr Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp
 20 25 30

Ile Phe Glu Leu Thr Gly Ala Ala Arg Lys Gly Ser Gly Arg Arg Leu
 35 40 45

Val Lys Gly Pro Asp Pro Ser Ser Pro Ala Phe Arg Ile Glu Asp Ala
 50 55 60

Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp Leu Val Asp
 65 70 75 80

Ala Val Arg Ala Glu Lys Gly Phe Leu Leu Leu Ala Ser Leu Arg Gln
 85 90 95

Met Lys Lys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His
 100 105 110

Ser Gly Gln Val Phe Ser Val Val Ser Asn Gly Lys Ala Gly Thr Leu
 115 120 125

Asp Leu Ser Leu Thr Val Gln Gly Lys Gln His Val Val Ser Val Glu
 130 135 140

Glu Ala Leu Leu Ala Thr Gly Gln Trp Lys Ser Ile Thr Leu Phe Val
 145 150 155 160

Gln Glu Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn
 165 170 175

Ala Glu Leu Asp Val Pro Ile Gln Ser Val Phe Thr Arg Asp Leu Ala
 180 185 190

Ser Ile Ala Arg Leu Arg Ile Ala Lys Gly Gly Val Asn Asp Asn Phe
 195 200 205

Gln Gly Val Leu Gln Asn Val Arg Phe Val Phe Gly Thr Thr Pro Glu
 210 215 220

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Asp Ile Leu Arg Asn Lys Gly Cys Ser Ser Ser Thr Ser Val Leu Leu
 225 230 235 240
 Thr Leu Asp Asn Asn Val Val Asn Gly Ser Ser Pro Ala Ile Arg Thr
 245 250 255
 Asn Tyr Ile Gly His Lys Thr Lys Asp Leu Gln Ala Ile Cys Gly Ile
 260 265 270
 Ser Cys Asp Glu Leu Ser Ser Met Val Leu Glu Leu Arg Gly Leu Arg
 275 280 285
 Thr Ile Val Thr Thr Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu
 290 295 300
 Asn Lys Glu Leu Ala Asn Glu Leu Arg Arg Pro Pro Leu Cys Tyr His
 305 310 315 320
 Asn Gly Val Gln Tyr Arg Asn Asn Glu Glu Trp Thr Val Asp Ser Cys
 325 330 335
 Thr Glu Cys His Cys Gln Asn Ser Val Thr Ile Cys Lys Lys Val Ser
 340 345 350
 Cys Pro Ile Met Pro Cys Ser Asn Ala Thr Val Pro Asp Gly Glu Cys
 355 360 365
 Cys Pro Arg Cys Trp Pro Ser Asp Ser Ala Asp Asp Gly Trp Ser Pro
 370 375 380
 Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys Gly Asn Gly Ile Gln
 385 390 395 400
 Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser
 405 410 415
 Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp Lys Arg Phe
 420 425 430
 Lys Gln Asp Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser
 435 440 445
 Val Thr Cys Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser
 450 455 460
 Pro Ser Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu
 465 470 475 480

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Thr Lys Ala Cys Lys Lys Asp Ala Cys Pro Ile Asn Gly Gly Trp Gly
485 490 495

Pro Trp Ser Pro Trp Asp Ile Cys Ser Val Thr Cys Gly Gly Gly Val
500 505 510

Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro Ala Pro Gln Phe Gly Gly
515 520 525

Lys Asp Cys Val Gly Asp Val Thr Glu Asn Gln Ile Cys Asn Lys Gln
530 535 540

Asp Cys Pro Ile Asp Gly Cys Leu Ser Asn Pro Cys Phe Ala Gly Val
545 550 555 560

Lys Cys Thr Ser Tyr Pro Asp Gly Ser Trp Lys Cys Gly Ala Cys Pro
565 570 575

Pro Gly Tyr Ser Gly Asn Gly Ile Gln Cys Thr Asp Val Asp Glu Cys
580 585 590

Lys Glu Val Pro Asp Ala Cys Phe Asn His Asn Gly Glu His Arg Cys
595 600 605

Glu Asn Thr Asp Pro Gly Tyr Asn Cys Leu Pro Cys Pro Pro Arg Phe
610 615 620

Thr Gly Ser Gln Pro Phe Gly Gln Gly Val Glu His Ala Thr Ala Asn
625 630 635 640

Lys Gln Val Cys Lys Pro Arg Asn Pro Cys Thr Asp Gly Thr His Asp
645 650 655

Cys Asn Lys Asn Ala Lys Cys Asn Tyr Leu Gly His Tyr Ser Asp Pro
660 665 670

Met Tyr Arg Cys Glu Cys Lys Pro Gly Tyr Ala Gly Asn Gly Ile Ile
675 680 685

Cys Gly Glu Asp Thr Asp Leu Asp Gly Trp Pro Asn Glu Asn Leu Val
690 695 700

Cys Val Ala Asn Ala Thr Tyr His Cys Lys Lys Asp Asn Cys Pro Asn
705 710 715 720

Leu Pro Asn Ser Gly Gln Glu Asp Tyr Asp Lys Asp Gly Ile Gly Asp
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725

730

735

Ala Cys Asp Asp Asp Asp Asp Asn Asp Lys Ile Pro Asp Asp Arg Asp
 740 745 750
 Asn Cys Pro Phe His Tyr Asn Pro Ala Gln Tyr Asp Tyr Asp Arg Asp
 755 760 765
 Asp Val Gly Asp Arg Cys Asp Asn Cys Pro Tyr Asn His Asn Pro Asp
 770 775 780
 Gln Ala Asp Thr Asp Asn Asn Gly Glu Gly Asp Ala Cys Ala Ala Asp
 785 790 795 800
 Ile Asp Gly Asp Gly Ile Leu Asn Glu Arg Asp Asn Cys Gln Tyr Val
 805 810 815
 Tyr Asn Val Asp Gln Arg Asp Thr Asp Met Asp Gly Val Gly Asp Gln
 820 825 830
 Cys Asp Asn Cys Pro Leu Glu His Asn Pro Asp Gln Leu Asp Ser Asp
 835 840 845
 Ser Asp Arg Ile Gly Asp Thr Cys Asp Asn Asn Gln Asp Ile Asp Glu
 850 855 860
 Asp Gly His Gln Asn Asn Leu Asp Asn Cys Pro Tyr Val Pro Asn Ala
 865 870 875 880
 Asn Gln Ala Asp His Asp Lys Asp Gly Lys Gly Asp Ala Cys Asp His
 885 890 895
 Asp Asp Asp Asn Asp Gly Ile Pro Asp Asp Lys Asp Asn Cys Arg Leu
 900 905 910
 Val Pro Asn Pro Asp Gln Lys Asp Ser Asp Gly Asp Gly Arg Gly Asp
 915 920 925
 Ala Cys Lys Asp Asp Phe Asp His Asp Ser Val Pro Asp Ile Asp Asp
 930 935 940
 Ile Cys Pro Glu Asn Val Asp Ile Ser Glu Thr Asp Phe Arg Arg Phe
 945 950 955 960
 Gln Met Ile Pro Leu Asp Pro Lys Gly Thr Ser Gln Asn Asp Pro Asn
 965 970 975

Trp Val Val Arg His Gln Gly Lys Glu Leu Val Gln Thr Val Asn Cys
 980 985 990

Asp Pro Gly Leu Ala Val Gly Tyr Asp Glu Phe Asn Ala Val Asp Phe
 995 1000 1005

Ser Gly Thr Phe Phe Ile Asn Thr Glu Arg Asp Asp Asp Tyr Ala
 1010 1015 1020

Gly Phe Val Phe Gly Tyr Gln Ser Ser Ser Arg Phe Tyr Val Val
 1025 1030 1035

Met Trp Lys Gln Val Thr Gln Ser Tyr Trp Asp Thr Asn Pro Thr
 1040 1045 1050

Arg Ala Gln Gly Tyr Ser Gly Leu Ser Val Lys Val Val Asn Ser
 1055 1060 1065

Thr Thr Gly Pro Gly Glu His Leu Arg Asn Ala Leu Thr His Thr
 1070 1075 1080

Gly Asn Thr Pro Gly Gln Val Arg Thr Leu Trp His Asp Pro Arg
 1085 1090 1095

His Ile Gly Trp Lys Asp Phe Thr Ala Tyr Arg Trp Arg Leu Ser
 1100 1105 1110

His Arg Pro Lys Thr Gly Phe Ile Arg Val Val Met Tyr Glu Gly
 1115 1120 1125

Lys Lys Ile Met Ala Asp Ser Gly Pro Ile Tyr Asp Lys Thr Tyr
 1130 1135 1140

Ala Gly Gly Arg Leu Gly Leu Phe Val Phe Ser Gln Glu Met Val
 1145 1150 1155

Phe Phe Ser Asp Leu Lys Tyr Glu Cys Arg Asp Pro
 1160 1165 1170

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Met Gly Leu Ala Trp Gly Leu Gly Val Leu Phe Leu Met His Val Cys
 Page 14

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5

15

Gly Thr

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<223> Thrombospondin Region plus N-terminal domain

<400> 40

Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp Ile Phe
1 5 10 15

Glu Leu Thr Gly Ala Ala Arg Lys Gly Ser Gly Arg Arg Leu Val Lys
20 25 30

Gly Pro Asp Pro Ser Ser Pro Ala Phe Arg Ile Glu Asp Ala Asn Leu
35 40 45

Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp Leu Val Asp Ala Val
50 55 60

Arg Ala Glu Lys Gly Phe Leu Leu Leu Ala Ser Leu Arg Gln Met Lys
65 70 75 80

Lys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His Ser Gly
85 90 95

Gln Val Phe Ser Val Val Ser Asn Gly Lys Ala Gly Thr Leu Asp Leu
100 105 110

Ser Leu Thr Val Gln Gly Lys Gln His Val Val Ser Val Glu Glu Ala
115 120 125

Leu Leu Ala Thr Gly Gln Trp Lys Ser Ile Thr Leu Phe Val Gln Glu
130 135 140

Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn Ala Glu
145 150 155 160

Leu Asp Val Pro Ile Gln Ser Val Phe Thr Arg Asp Leu Ala Ser Ile
165 170 175

Ala Arg Leu Arg Ile Ala Lys Gly Gly Val Asn Asp Asn Phe Gln Gly
180 185 190

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Val Leu Gln Asn Val Arg Phe Val Phe Gly Thr Thr Pro Glu Asp Ile
195 200 205

Leu Arg Asn Lys Gly Cys Ser Ser Ser Thr Ser Val Leu Leu Thr Leu
210 215 220

Asp Asn Asn Val Val Asn Gly Ser Ser Pro Ala Ile Arg Thr Asn Tyr
225 230 235 240

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<400> 41

Ile Gly His Lys Thr Lys Asp Leu Gln Ala Ile Cys Gly Ile Ser Cys
1 5 10 15

Asp Glu Leu Ser Ser Met
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<223> Thrombospondin region plus procollagen homology domain

<400> 42

Val Leu Glu Leu Arg Gly Leu Arg Thr Ile Val Thr Thr Leu Gln Asp
1 5 10 15

Ser Ile Arg Lys Val Thr Glu Glu Asn Lys Glu Leu Ala Asn Glu Leu
20 25 30

Arg Arg Pro Pro Leu Cys Tyr His Asn Gly Val Gln Tyr Arg Asn Asn
35 40 45

Glu Glu Trp Thr Val Asp Ser Cys Thr Glu Cys His Cys Gln Asn Ser
50 55 60

Val Thr Ile Cys Lys Lys Val Ser Cys Pro Ile Met Pro Cys Ser Asn
65 70 75 80

Ala Thr Val Pro Asp Gly Glu Cys Cys Pro Arg Cys Trp Pro Ser Asp
Page 16

Ser Ala

<210> 43
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<212> PRT
<213> Artificial

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<223> Thrombospondin region plus domain of type 1 repeats

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Asp Asp Gly Trp Ser Pro Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser
1 5 10 15

Cys Gly Asn Gly Ile Gln Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn
20 25 30

Asn Arg Cys Glu Gly Ser Ser Val Gln Thr Arg Thr Cys His Ile Gln
35 40 45

Glu Cys Asp Lys Arg Phe Lys Gln Asp Gly Gly Trp Ser His Trp Ser
50 55 60

Pro Trp Ser Ser Cys Ser Val Thr Cys Gly Asp Gly Val Ile Thr Arg
65 70 75 80

Ile Arg Leu Cys Asn Ser Pro Ser Pro Gln Met Asn Gly Lys Pro Cys
85 90 95

Glu Gly Glu Ala Arg Glu Thr Lys Ala Cys Lys Lys Asp Ala Cys Pro
100 105 110

Ile Asn Gly Gly Trp Gly Pro Trp Ser Pro Trp Asp Ile Cys Ser Val
115 120 125

Thr Cys Gly Gly Gly Val Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro
130 135 140

Ala Pro Gln Phe Gly Gly Lys Asp Cys Val Gly Asp Val Thr Glu Asn
145 150 155 160

Gln Ile Cys Asn Lys Gln Asp Cys Pro Ile
165 170

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<400> 44

Asp Gly Cys Leu Ser Asn Pro Cys Phe Ala Gly Val Lys Cys Thr Ser
1 5 10 15

Tyr Pro Asp Gly Ser Trp Lys Cys Gly Ala Cys Pro Pro Gly Tyr Ser
20 25 30

Gly Asn Gly Ile Gln Cys Thr Asp Val Asp Glu Cys Lys Glu Val Pro
35 40 45

Asp Ala Cys Phe Asn His Asn Gly Glu His Arg Cys Glu Asn Thr Asp
50 55 60

Pro Gly Tyr Asn Cys Leu Pro Cys Pro Pro Arg Phe Thr Gly Ser Gln
65 70 75 80

Pro Phe Gly Gln Gly Val Glu His Ala Thr Ala Asn Lys Gln Val Cys
85 90 95

Lys Pro Arg Asn Pro Cys Thr Asp Gly Thr His Asp Cys Asn Lys Asn
100 105 110

Ala Lys Cys Asn Tyr Leu Gly His Tyr Ser Asp Pro Met Tyr Arg Cys
115 120 125

Glu Cys Lys Pro Gly Tyr Ala Gly Asn Gly Ile Ile Cys Gly Glu
130 135 140

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3 repeat

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Asp Thr Asp Leu Asp Gly Trp Pro Asn Glu Asn Leu Val Cys Val Ala
1 5 10 15

Asn Ala Thr Tyr His Cys Lys Lys
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<400> 46

Asp Asn Cys Pro Asn Leu Pro Asn Ser Gly Gln Glu Asp Tyr Asp Lys
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Asp Gly Ile Gly Asp Ala Cys Asp Asp Asp Asp Asn Asp Lys Ile
 20 25 30

Pro Asp Asp Arg
 35

<210> 47
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<400> 47

Asp Asn Cys Pro Phe His Tyr Asn Pro Ala Gln Tyr Asp Tyr Asp Arg
 1 5 10 15

Asp Asp Val Gly Asp Arg Cys
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<210> 48
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<400> 48

Asp Asn Cys Pro Tyr Asn His Asn Pro Asp Gln Ala Asp Thr Asp Asn
 1 5 10 15

Asn Gly Glu Gly Asp Ala Cys Ala Ala Asp Ile Asp Gly Asp Gly Ile
 20 25 30

Leu Asn Glu Arg
 35

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Asp Asn Cys Gln Tyr Val Tyr Asn Val Asp Gln Arg Asp Thr Asp Met
1 5 10 15

Asp Gly Val Gly Asp Gln Cys
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<400> 50

Asp Asn Cys Pro Leu Glu His Asn Pro Asp Gln Leu Asp Ser Asp Ser
1 5 10 15

Asp Arg Ile Gly Asp Thr Cys Asp Asn Asn Gln Asp Ile Asp Glu Asp
20 25 30

Gly His Gln Asn Asn Leu
35

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<220>
<223> Thrombospondin region

<400> 51

Asp Asn Cys Pro Tyr Val Pro Asn Ala Asn Gln Ala Asp His Asp Lys
1 5 10 15

Asp Gly Lys Gly Asp Ala Cys Asp His Asp Asp Asp Asn Asp Gly Ile
20 25 30

Pro Asp Asp Lys
35

<210> 52
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Asp Asn Cys Arg Leu Val Pro Asn Pro Asp Gln Lys Asp Ser Asp Gly
1 5 10 15

Asp Gly Arg Gly Asp Ala Cys Lys Asp Asp Phe Asp His Asp Ser Val
20 25 30

Pro Asp Ile Asp
35

<210> 53
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<212> PRT
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<220>
<223> Thrombospondin Region plus C-terminal domain

<400> 53

Asp Ile Cys Pro Glu Asn Val Asp Ile Ser Glu Thr Asp Phe Arg Arg
1 5 10 15

Phe Gln Met Ile Pro Leu Asp Pro Lys Gly Thr Ser Gln Asn Asp Pro
20 25 30

Asn Trp Val Val Arg His Gln Gly Lys Glu Leu Val Gln Thr Val Asn
35 40 45

Cys Asp Pro Gly Leu Ala Val Gly Tyr Asp Glu Phe Asn Ala Val Asp
50 55 60

Phe Ser Gly Thr Phe Phe Ile Asn Thr Glu Arg Asp Asp Asp Tyr Ala
65 70 75 80

Gly Phe Val Phe Gly Tyr Gln Ser Ser Ser Arg Phe Tyr Val Val Met
85 90 95

Trp Lys Gln Val Thr Gln Ser Tyr Trp Asp Thr Asn Pro Thr Arg Ala
100 105 110

Gln Gly Tyr Ser Gly Leu Ser Val Lys Val Val Asn Ser Thr Thr Gly
115 120 125

Pro Gly Glu His Leu Arg Asn Ala Leu Trp His Thr Gly Asn Thr Pro
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130

135

Gly Gln Val Arg Thr Leu Trp His Asp Pro Arg His Ile Gly Trp Lys
145 150 155 160

Asp Phe Thr Ala Tyr Arg Trp Arg Leu Ser His Arg Pro Lys Thr Gly
165 170 175

Phe Ile Arg Val Val Met Tyr Glu Gly Lys Lys Ile Met Ala Asp Ser
180 185 190

Gly Pro Ile Tyr Asp Lys Thr Tyr Ala Gly Gly Arg Leu Gly Leu Phe
195 200 205

Val Phe Ser Gln Glu Met Val Phe Phe Ser Asp Leu Lys Tyr Glu Cys
210 215 220

Arg Asp Pro
225

<210> 54
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<400> 54

Cys Ser Val Thr Cys Gly
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<210> 55
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Arg Phe Tyr Val Val Met Trp Lys
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<400> 56

Arg Phe Tyr Val Val Met
1 5

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<400> 57

Phe Tyr Val Val Met Trp Lys
1 5

<210> 58

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<400> 58

Ile Arg Val Val Met
1 5

<210> 59

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